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| 08/203,004 | 02/28/1994 | DAVID BERD | 061266-5001-03 | 2699 |

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MORGAN, LEWIS & BOCKIUS LLP
1701 MARKET STREET
PHILADELPHIA, PA 19103-2921

| EXAMINER | |
|---|---|
| UNGAR, SUSAN NMN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |
| **MAIL DATE** | **DELIVERY MODE** |
| 01/09/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 08/203,004 | BERD, DAVID | |
| | Examiner | Art Unit | |
| | Susan Ungar | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *13 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *47,67,68,70,72,74,75 and 77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *47, 67-68, 70, 72, 74-75, 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Amendment filed November 13, 2007 in response to the Office Action of May 11, 2007 is acknowledged and has been entered. Previously pending claims 43-44, 49-62, 64-66, 69, 71, 76 have been canceled, claims 47, 70, 75, 77 have been amended. Claims 47, 67-68, 70, 72, 74-75, 77 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 47, 67-68, 70, 72, 74-75, 77 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed May 11, 2007, Section 8, pages 12-13.

Applicant argues that amendment of claim 47 obviates the instant rejection. Applicant points to support for the limitation "repeating said administration at least six times" at page 27, lines 22-28, page 31, line 22 to p 32 line 11 and p. 41, lines 22-24. The argument has been considered but has not been found persuasive because a review of page 27, lines 22-28 reveals support only for;

> "On day 0, patients received cyclophosphamide 300 mg/M2 as a rapid i.v. infusion. Three days later, on day +3, they were injected intradermally with

autologous melanoma vaccine. Additional vaccine injections were administered every four weeks for a total of eight treatments. Cyclophosphamide was given only prior to the first two injections. All vaccines were DNP-conjugated....."

A review of page 31, line 22 to p. 32 line 11 reveals support only for;

"Patients were pre-treated with cyclophosphamide 300 mg/M2, see Berd et al. (1986) supra, and three days later were sensitized to DNFB by topical application of 0.i ml of a 1 DNFB solution in acetone-corn oil on two consecutive days. Two weeks later patients were again given cyclophosphamide, followed 3 days later by injection of DNP-conjugated melanoma vaccine. DNP-vaccine was repeated every 28 days. Cyclophosphamide was given prior to the first two cycles. The vaccine consisted of i0 x 106 - 25 x 106 cryopreserved, autologous, irradiated (2500 R), DNP-conjugated melanoma cells conjugated to DNP mixed with BCG.All tumor preparations contained lymphocytes which were the residua of tumor-infiltrated lymph node tissue. Serum and PBL were collected at the following time points: day 0 (before sensitization), day 14 (2 weeks after DNFB sensitization), day 63 (after 2 vaccines), day 119 (after vaccines), day 175 (after 6 vaccines), and day 231 (after 8 vaccines)."

A review of page 41, lines 22-24 reveals support only for;

"They were injected i.d. every 28 days for a total of 8 treatments. Cyclophosphamide 300 mg/M2 i.v. was given 3 days before the first 2 vaccines only. The DFS and TS of these patients were compared with those of 22 melanoma patients with resected nodal metastases treated previously with an unconjugated vaccine"

The suggested support has been considered but has not been found persuasive because none of the citations support the claim limitation drawn to at least six administrations. In each case 8 treatments were administered, there is neither guidance nor suggestion of "at least six" and although the 8 treatments are clearly more than six, it is clear that the limitation of "at least six" was never contemplated in the specification as originally filed.

Applicant's arguments have not been found persuasive and the rejection is maintained.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 47, 67-68, 70, 72, 74-75, 77 remain rejected under 35 USC 103 for the reasons previously set forth in the paper mailed May 11, 2007, Section 17, pages 26-38.

Applicant argues that independent claim 47 has been amended to recite "repeating said administration of said composition for a total of at least six administrations of said composition and administering a therapeutically effect amount of cyclophosphamide to the patient only prior to the first administration of said composition", dependent claim 70 has been amended to recite "wherein

administering a therapeutically effective amount of cyclophosphamide comprises administering a dose of about 300 mg/M2 of cyclophosphamide prior to the first administration of said composition and that these amendments obviate the instant rejection. Applicant specifically argues that none of the references relied upon, either alone or in combination, disclose, teach, or suggest the claimed method comprising administering hapten-conjugated autologous tumor cells, repeating the administration for a total of at least six administrations of the composition, and administering a therapeutically effective amount of cyclophosphamide only prior to the administration of the composition as required by the claims.

The argument has been considered but has not been found persuasive because a review of the instant rejection reveals that Berd et al specifically teach a successful method of treating melanoma comprising administering 300 mg/M2 of cyclophosphamide prior to the first administration of DNP haptenized autologous irradiated melanoma cells which in combination with the other references cited make obvious the claimed invention for the reasons of record. Further it is noted that Berd et al only teach administration of cyclophosphamide prior to the first administration of DNP haptenized autologous melanoma cells. In addition, as previously set forth the teachings of US Patent No. 5,008,183, which teaches conventional immunizing protocols, in combination with the other references cited makes obvious the claimed invention for the reasons of record.

***Obviousness-Type Double Patenting***

8. Claims 47, 67-68, 70, 74 remain rejected under the judicially created doctrine of obviousness-type double patenting for the reasons previously set forth in the paper mailed May 11, 2007, Section 13, pages 15-17.

Applicant states that the filing of a Terminal Disclaimer directed to US Patent No. 6,458,369 is deferred until one or more claims is considered allowable by the Examiner. Accordingly, Applicant requests that this rejection be withdrawn.

The statement is noted but is not found persuasive, Applicant has not filed the Terminal Disclaimer and the rejection is maintained for the reasons of record.

***New Grounds of Rejection***

9. Claims 47, 67-68, 70, 72, 74-75, 77 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of "administering.....only prior to the first administration of said composition" recited in claim 47 has no clear support in the specification and the claims as originally filed. Applicant points to support for the newly claimed limitation at page 27, lines 22-28, page 31, line 22 to p 32 line 11 and p. 41, lines 22-24. However, a review of page 27, lines 22-28 reveals support only for;

> "On day 0, patients received cyclophosphamide 300 mg/M2 as a rapid i.v. infusion. Three days later, on day +3, they were injected intradermally with autologous melanoma vaccine. Additional vaccine injections were administered every four weeks for a total of eight treatments. Cyclophosphamide was given only prior to the first two injections. All vaccines were DNP-conjugated....."

A review of page 31, line 22 to p. 32 line 11 reveals support only for;

> "Patients were pre-treated with cyclophosphamide 300 mg/M2, see Berd et al. (1986) supra, and three days later were sensitized to DNFB by topical application of 0.i ml of a 1 DNFB solution in acetone-corn oil on two

consecutive days. Two weeks later patients were again given cyclophosphamide, followed 3 days later by injection of DNP-conjugated melanoma vaccine. DNP-vaccine was repeated every 28 days. Cyclophosphamide was given prior to the first two cycles. The vaccine consisted of i0 x 106 - 25 x 106 cryopreserved, autologous, irradiated (2500 R), DNP-conjugated melanoma cells conjugated to DNP mixed with BCG.All tumor preparations contained lymphocytes which were the residua of tumor-infiltrated lymph node tissue. Serum and PBL were collected at the following time points: day 0 (before sensitization), day 14 (2 weeks after DNFB sensitization), day 63 (after 2 vaccines), day 119 (after vaccines), day 175 (after 6 vaccines), and day 231 (after 8 vaccines)."

A review of page 41, lines 22-24 reveals support only for;

"They were injected i.d. every 28 days for a total of 8 treatments. Cyclophosphamide 300 mg/M2 i.v. was given 3 days before the first 2 vaccines only. The DFS and TS of these patients were compared with those of 22 melanoma patients with resected nodal metastases treated previously with an unconjugated vaccine"

The suggested support has been considered but has not been found persuasive because none of the citations support the claim limitation drawn to "only prior to". Although in each case, the cyclophosphamide was administered prior to the composition, there is neither guidance on, nor suggestion of the claimed limitation and it is clear that the instant limitation was never contemplated in the specification as originally filed. The subject matter claimed in claims 47, 67-68, 70, 72, 74-75, 77 broadens the scope of the invention as originally disclosed in the specification.

9. No claims allowed.

10. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited

either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

11. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at 571-272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Susan Ungar
Primary Patent Examiner
January 7, 2008